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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/026,914	12/27/2001	Birgit Linhart	966927.00006	6890

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EXAMINER	
HINES, JANA A	
ART UNIT	PAPER NUMBER
1645	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/026,914	LINHART ET AL.	
	Examiner	Art Unit	
	JaNa Hines	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 October 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7,9,22-25,36-47,52 and 53* is/are pending in the application.

4a) Of the above claim(s) *7,9,22-25,36-41 and 44* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *42,43,45-47,52 and 53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Amendment Entry

1. The amendment filed October 26, 2009 has been entered. Claims 1-6, 8, 10-21, 26-35 and 48-51 are cancelled. Claims 7, 9, 22-25, 36- 41 and 44 are withdrawn from consideration. Claims 42-43 and 45-47 have been amended. Claims 52-53 have been newly added. Claims 45-47 and 52-53 are under consideration in this office action.

2. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Withdrawal of Rejections

3. The following rejections have been withdrawn in view of applicants' amendments and arguments:

a) The rejection of claims 42-43 and 45-47 under 35 U.S.C. 103(a) as being unpatentable over Ball et al., in view of Vrtala et al;

b) The rejection of claim 45 under 35 U.S.C. 102(b) as being anticipated by Ball et al (WO 95/34578);

c) The rejection of claim 45 under 35 U.S.C. 102(b) as being anticipated by Ball et al (US Patent 6,008,340); and

d) The rejection of claims 42-43 and 45-47 under 35 U.S.C. 103(a) as being unpatentable over Ball et al.,(US Patent 6,008,340) in view of Vrtala et al.

Response to Arguments

4. Applicant's arguments, filed October 26, 2009, with respect to the rejection(s) of claim(s) 42-43 and 45-47 under 35 U.S.C. 102(b) and 35 U.S.C. 103(a) have been fully considered and are persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, a new ground(s) of rejection is made.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 42-43 and 45-47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mudde (WO 1997/007218) in view of Vrtala et al., (1996. J. Allergy Clin Immun. Vol.97(3):781-787).

Claim 42 is drawn to a method of preparing fusion allergens consisting of recombinant polypeptides of two or more different naturally occurring timothy grass pollen allergens for use as immunotherapeutic agents comprising: (a) providing a polynucleotide sequence encoding the fusion allergen; (b) introducing said polynucleotide sequence into a host cell; (c) culturing the host cell obtained in b) under conditions such that the fusion allergen is expressed; and (d) recovering the expressed fusion polypeptide allergen from the cultured host cell; (e) testing the fusion allergen as candidate immunotherapeutic agents by administering said allergen to a test animal and

selecting as immunotherapeutic agents those fusion allergens that induce IgE-blocking antibodies and induce stronger immune responses compared with the individual components or fragments thereof.

Claim 45 is drawn to a pharmaceutical composition comprising one or more fusion allergens of timothy grass pollen allergens as immunotherapeutic agents, wherein said agents consists of recombinant fusion allergens of two or more different naturally occurring timothy grass pollen allergens which have been identified by a method comprising the steps of: (a) providing fusion allergens of naturally occurring timothy grass pollen allergens; (b) challenging an immunological model with said fusion allergens; (c) selecting as candidate immunotherapeutic agents, those fusion allergens which induce IgE-blocking antibodies and induce stronger immune responses compared with the respective allergens which comprise the fusion allergen. Claim 46 is drawn to a fusion allergen for treatment of IgE-mediated hypersensitivity, wherein said fusion allergen consists of two or more different timothy grass pollen allergens.

Mudde teaches complexes of human IgG and antigen/allergen or a combination of antigens/allergens. It concerns fusion proteins between anti-CD32 molecules and a combination of antigens/allergens (page 1, para .1). Allergens are defined herein as antigens to which atopic patients respond with allergic reactions. Antigens as used herein can be of various origins, e.g. environmental allergens (e.g. house dust mite, birch pollen, grass pollen, cat antigens, cockroach antigens), or food allergens or a combination of both, or non-relevant antigens (page 1, para .1). Mudde teaches complexes including the CD32/antigen fusion proteins direct the immune response to

cells of the monocytic and dendritic cell lineage, which induce T cell responses of mainly Th1 type B cells (page 3, para 3). Mudde teaches fusion proteins comprising a) one or more antigens and b) one or more moieties, such as from antibody molecules, interacting with human Fcγ receptor π (FcγRLI) (CD32), hereinafter briefly named "the fusion proteins according to the invention." (page 4, para. 3). The antigens may be from complete proteins or parts thereof still having epitopes for T cells on the sequences present in the fusion protein (page 6, para 1). Any antigen to which allergic patients respond with IgE-mediated hypersensitivity reactions can be used, including the most common environmental allergens such as grass pollen and including allergens having one or more "major allergens." (page 6, para. 1).

Mudde teaches the fusion between aCD32 and antigens can be affected at the gene level i.e., the recombinant fusion protein, and the invention also comprises a process for producing fusion proteins; where it is carried out in conventional manner, and preferably comprises the use of recombinant gene techniques or chemical cross-linking (page 7, para. 1). Mudde teaches that recombinant fusion proteins are preferred (page 7, para .1). The fusion proteins according to the invention are useful for the prevention and/or treatment of allergies (page 9, para. 1). It is not uncommon for patients who suffer from anaphylactic response to a particular allergen, also to suffer from such a response to one or more other allergens (page 9, para 1). It is possible by the method of the present invention to desensitize such a patient in respect of two or more allergens simultaneously by administering a fusion protein including antigens against each of these allergens (page 9, para. 1). Preferably the fusion proteins

according to the invention will be used for the prevention and/or treatment of allergy or of established allergies in patients with allergy against the allergens which is are included in the particular fusion protein used (page 9, para. 1). Mudde teaches the administration of the fusion protein as an immunotherapeutic for the prevention and/or treatment of allergies (page 9, para. 3). While Mudde teaches the inclusion of different grass allergens, while Mudde does not recite timothy grass pollen allergens.

Vrtala et al., teach grass pollen allergens belong to the potent elicitors of type I allergy (abstract). Vrtala et al., teach that DNA coding for three major timothy grass pollen allergens representing group I (Phl p1), group II (Phl p 2) and group V (Phl p 5) was known (page 781). There is no relevant immunologic similarity between Phl p 2 and Phl p 1(page 781). Vrtala et al., teach *B*-galactosidase fusion proteins from the above-mentioned grass pollen allergens were successfully used to diagnose grass pollen allergy in individuals and it demonstrated that the recombinant Phl p1, Phl p2 and Phl p5 can be used to determine the sensitization patterns (page 781). Vrtala et al., teach mature allergen encoding cDNA and showed considerable improvement in the diagnosis of grass pollen allergy when recombinant allergens are used along with improvements for specific immunotherapy (page 782). The methods section teaches the construction of the expression plasmids for Phl p 1, Phl p 2 and Phl p 5.(page 782). cDNA clones were transcribed by polymerase chain reaction to DNA fragments coding for the mature allergens (page 782). Phl p 1 and Phl p 2, both of which contained ATG start codon in front of the coding region of the mature protein and genes were then inserted as fragments (page 782). The plasmids were transfected into *E.coli* host cells.

The expression of the recombinant allergens in *E.coli* was also taught wherein cells were cultured, expressed, purified and thereby recovered (page 782).

Therefore it would have been prima facie obvious at the time of applicants' invention to modify the fusion allergens as taught by Mudde to include timothy grass pollen allergens as taught by Vrtala et al., since Mudde already teach fusion grass pollen allergens having different allergens for use as immunotherapeutic, along with a method of preparation, in order to provide improvements for specific timothy grass pollen immunotherapy. Mudde teach that grass pollen allergens amenable to being fusion allergens while Vrtala et al., teach timothy grass pollen allergens are known in the art to be expressed within fusion proteins; thus no more than routine skill would have been required to combine the elements as claimed by well known methods with no change in their respective functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the inventions. Finally, there is a reasonable expectation of success in using the recombinant timothy grass allergens of Vrtala et al., when the Mudde teach that all of these grass pollen allergens can be expressed as a fusion allergens and administered as an immunotherapeutic in association with the prevention and/or treatment of allergies.

Conclusion

7. It is noted that claims 52 and 53 are drawn to allowable subject matter, however claims 52 and 53 are dependant upon rejected claims 42 and 45, thus the claims are objected to.

8. No claims allowed.

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is 571-272-0859. The examiner can normally be reached Monday thru Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Robert Mondesi, can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/JaNa Hines/
Examiner, Art Unit 1645

/Mark Navarro/
Primary Examiner, Art Unit 1645